Kindly amend claim 4 by inserting a period at the end of the claim.

Kindly amend claim 13, lines 1 and 2 by deleting the phrase "introducing a combined immunization medication program".

REMARKS

Claims 1 to 20 remain in the application.

Reconsideration and re-examination of the application on the basis of the claims as amended and the following remarks is respectfully requested.

Claim 4 has been amended to include the period to overcome the informality objection.

Claims 13 to 20 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite. As suggested by the Examiner, the claims have been amended to recite a method for protecting poultry birds against coccidiosis comprising.

Claims 1 to 4 have been rejected under 35 U.S.C. 112, second paragraph as being indefinite. These claims have been amended to be directed to a method of protecting an animal against a chronic infection caused by an infectious organism which undergoes more than one life cycle.

With the above amendments it is respectfully submitted that the objection and rejections of the claims under 35 U.S.C. 112 have been overcome.

Claims 1 to 20 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Bafundo et al. in view of Andrews et al. and Crane et al. The Examiner was of the view that the claims in the present invention were *prima facie* obvious in view of combination of Bafundo et al. and Andrews et al. and Crane et al. Applicant respectfully traverses the rejection.

The present invention is directed to a method of protecting an animal against a chronic infection caused by an infectious organism which undergoes more than one life cycle. The method comprises administering to the animal a vaccine containing sufficient organisms to develop an immunological response in the animal. The animal is maintained free from chemotherapeutic agents effective against the infectious organism for a period of time corresponding to about one life cycle of the organism. Thereafter, the animal is administered a chemotherapeutic agent effective against the infectious organisms for a period of time corresponding to at least one life cycle of the infectious organism. As set forth in the present application on pages 10-12, this method permits the animal to be exposed to the entire antigenic compliment of the organism to enable it to develop the full immunological response to the infective organism before the commencement of chemotherapy. The commencing of the chemotherapeutic agent treatment during the second life cycle of the organism allows recycling to occur in the animals such that they are exposed to the organism shed at the end of the first life cycle. The administration of the chemotherapeutic agent limits the effects to the animal from the live vaccine particularly effects evident after the first life cycle of the infectious organism. It is respectfully submitted that the method of the claims and the advantages is not suggested let alone taught by the cited reference either alone or in combination.

Bafundo et al. teaches a method for protecting an animal against coccidiosis comprising administering to the animal a vaccine, maintaining the animal free of any chemotherapeutic agents for a period beginning with birth or hatching and continuing until sporozoites have penetrated host cells, and thereafter administering a chemotherapeutic agent. The chemotherapeutic agent is administered substantially continuously throughout the life of the animal. Bafundo teaches that the length of delay before administering the chemotherapeutic agent or ionophore should be extremely short, only long enough to permit the coccidia to travel to the relevant section of the intestinal track and invade the host cells. As set forth in the paragraph beginning in column 4, line 45 of Bafundo:

> "the exact number of hours of delay will vary with the identity of the host and the rate of transit through the gastrointestinal tract; and with the particular species of coccidium and the location of the gastrointestinal tract which it infects. In chickens this delay should be on the general order of one to four hours. In cattle, it is expected that the delay be on the order of 4 to 8 hours. It is possible to delay chemotherapeutic treatment for an even longer time period such as up to 24 hours. However, further delay leaves the animal unprotected from coccidiosis, except as has been provided by the immunological process, and is therefore undesirable. The preferred practice, therefore, is to delay ionophore therapy only as long as the time required for sporozoites to penetrate the host cells."

Thus, Bafundo clearly teaches that the commencement of the ionophore or chemotherapeutic agent therapy must start no later than 24 hours after immunization. Delaying beyond this time, the commencement of chemotherapeutic therapy would be going against the teaching of Bafundo.

The Examiner cited Andrews et al. as teaching antigenic proteins capable of inducing in a chicken an immune response conferring protection against Eimeria tenella and that these proteins are found in the sporocyst stage of the life cycle. Crane et al. has been cited as teaching the cross protection against four species of chicken coccidia with a single recombinant antigen. The Examiner also cited this reference as teaching that the protection induced by "B antigen immunization is not sufficient to compete with prophylactic chemotherapy and that even in high doses does not induce sterile immunity nor does it fully prevent disease". It is to be noted that the Examiner did not include the first portion of this quotation: "However in contrast to the live vaccination..." which changes the meaning substantially.

Both of these references are directed to the identification of specific antigens of Eimeria species in the hopes of being able to develop a subunit vaccine which would not require the administration of live organisms to the poultry. There are however problems associated with subunit vaccine and in most cases they do not perform as well as live vaccine. As stated by Crane et al. on page 1274, second column, last paragraph:

> "It is well established that infection with virulent or attenuated strains of coccidia induces strong, species-specific, protective immunity in chickens".

And in respect to the specific "B" antigen studied in his study he states on page 1275, second column,

> "However, in contrast to the live vaccination, B antigen, even at relatively high doses does not induce sterile immunity nor does it fully prevent disease. These results indicate some fundamental differences between immunity induced by mild infection and that induced by the B antigen: it would appear that the B antigen is not involved in establishing species-specific immunity effected by live infection."

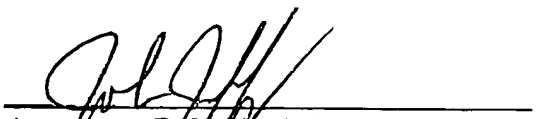
While all of the references cited by the Examiner are directed to coccidiosis infection in poultry it is respectfully submitted that one of skill in the art would not be led to combine them in the manner suggested by the Examiner. All of the references cited by the Examiner recognize the high levels of protection available utilizing live vaccine, see for example, Crane et al. page 1275 and Andrews et al. column 3. And one of skill in the art would not choose an inferior subunit vaccine over live vaccine. However if one were to combine the teaching of the cited art at best to one of skill in the art, the teaching of Andrews et al. or Crane et al. would provide for the substitution of the live vaccine of Bafundo with the subunit vaccine once one is successfully developed. Thus, the combination of Andrews et al. or Crane et al. with Bafundo et al. would lead one of skill in the art to utilize a subunit vaccine for immunization of the animals in replacement of the live vaccine of Bafundo. The so immunized animals would then be started on the chemotherapeutic agent no later than 24 hours after the immunization. In fact, it is the Applicant's submission that as the subunit vaccine of Andrews et al. or Crane et al. would not include live organisms, it would no longer be necessary to wait until the organism had penetrated the host cells. As no live organism would be present, one of skill in the art combining the teaching of Andrews et al., Crane et al. and Bafundo et al. would, upon utilizing the subunit vaccine, immediately commence administration of the chemotherapeutic agent and continue the administration of this stage

substantially continuously throughout the life of the animal. Combining the teaching of Andrews et al., Crane et al. and Bafundo et al. would not lead one to wait until the completion of the infectious agent life cycle before the administration of the chemotherapeutic agent. Delaying this administration would be clearly ignoring the teaching of Bafundo that the earliest possible use of the ionophores, no later than 24 hours after immunization, is essential for the practicing of his invention. In addition, if no live organisms were present, it would not be necessary or in fact possible to wait for the completion of one life cycle. To delay the introduction of the ionophore or other therapeutic agent beyond 24 hours would require that one go against the teaching of Bafundo to the point of exercising inventive ingenuity as it would have been obvious to one of skill in the art from the teaching of Bafundo that an essential element of his invention isto administer the chemotherapeutic agent within 24 hours.

Accordingly, in view of all the above, it is respectfully submitted that the cited references do not establish that the claims of the present application are obvious, let alone *prima facie* obvious. Rather the proper application of the cited references clearly shows that the present claims define a patentable invention over the art.

In view of all the above, it is respectfully submitted that the application is allowable and early allowance it is hereby requested.

Respectfully submitted



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